REMARKS

Prior to entry of the present amendment, claims 1-37 are pending. Claims 1-11, 14-17, 19-22, 24-26, and 28-37, due to a Restriction Requirement, are withdrawn from consideration. The specification is objected to. Claims 12, 13, 23, and 27 are objected to, claims 12, 13, 18, 23, and 27 are rejected under 35 U.S.C. § 112, first paragraph, claims 13, 18, 23, and 27 are rejected under 35 U.S.C. § 112, second paragraph, and claims 12, 13, 18, 23, and 27 are rejected under 35 U.S.C. § 102. Applicants address each of these bases for objection or rejection as follows.

Amendments

Claim 12 has been amended to recite a peptide of 5 to 20 amino acids, where the peptide includes a sequence that, over its full length, is at least 82% identical to the amino acid sequence EATVGERVRL (SEQ ID NO:2) of vascular endothelial growth factor receptor (VEGFR). Support for this amendment is found in the specification as filed, for example, at page 6 (paragraph 20), page 10 (paragraph 31), page 13 (paragraph 38), page 14 (paragraph 41), Table 1, and Figure 13. Claim 12 has also been amended to recite that contacting a cell expressing a VEGFR with the peptide decreases proliferation of the cell relative to a control cell not contacted with the peptide or inhibits neovascularization relative to a control not contacted with the peptide. Support for this amendment is found, for example, at pages 30-31 (paragraphs 89, 90, and 91) of the specification and in

Figures 2A, 2B, and 2C.

Claim 18 has been re-written in independent form and has been amended to recite that the method involves contacting a cell with a peptide of 5 to 20 amino acids, where the peptide includes a sequence that, over its full length, is at least 82% identical to the amino acid sequence of SEQ ID NO:2, where a decrease in proliferation of the cell relative to a control cell not contacted with the peptide is indicative of the peptide inhibiting VEGFR activity. Support for this amendment is found in the specification as filed, for example, at page 6 (paragraph 20), page 10 (paragraph 31), page 13 (paragraph 38), page 14 (paragraph 41), page 30 (paragraphs 89 and 90), in Table 1, and in Figures 2A, 2B, and 13.

New claims 38-41 have been added. Support for new claims 38 and 40 is found, for example, at page 13 (paragraph 38) of the specification, support for new claim 39 is found, for example, in Table 1 of the specification, and support for new claim 41 is found, for example, at pages 30-31 (paragraph 91) of the specification and in Figure 2C.

In view of the amendment to claim 12, claim 13 has been canceled, and in view of the amendment to claim 18, claim 23 has been canceled. In addition, withdrawn claims 1-11, 14-17, 19-22, 24-26, and 28-37 and claim 27 have been canceled.

Further, the specification has been amended to include sequence identifiers in the Brief Description of the Drawings and to correct minor typographical errors.

No new matter has been added by the present amendment.

Applicants reserve the right to pursue any canceled subject matter in this or in a continuing application.

Objection to the Specification

The specification is objected to because "the sequences disclosed in Figures 3-7 and 11-13 are not accompanied by the required sequence identifiers." In response, the Brief Description of the Drawings for Figures 3-7 and 11-13 has been amended to include sequence identifiers for all nucleic acid and amino acid sequences shown in these figures. This basis for objection may be withdrawn.

Objection to the Claims

The Office suggests amending claim 12 to replace the term "containing" with the term "comprising." Applicants submit that, in view of the present amendment to claim 12, this objection is moot.

Claims 13, 23, and 27 are objected to for reciting non-elected subject matter.

Claims 13, 23, and 27 have been canceled. Applicants submit that the claims as amended are directed to the elected subject matter. This basis for objection may be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 12, 13, 18, 23, and 27 are rejected under 35 U.S.C. § 112, first paragraph,

for an asserted lack of enablement and written description in the specification as filed.

Claims 13, 23, and 27 have been canceled and rejection of these claims, therefore, is moot. Applicants address these bases for rejection as they apply to the amended claims as follows.

Enablement

In rejecting claims 12, 13, 18, 23, and 27 for lack of enablement, the Office states that the specification "while being enabling for the cytokine receptor peptide antagonists described in the examples of the specification, does not reasonably provide enablement for any other peptide antagonists 'derived from' a cytokine receptor." Applicants submit that the claims as amended are free of this basis for rejection.

As noted above, claims 12 and 18 have been amended to recite a peptide of 5 to 20 amino acids, where the peptide includes a sequence that, over its full length, is at least 82% identical to the amino acid sequence EATVGERVRL (SEQ ID NO:2) of VEGFR. In addition, claims 12 and 18 require that contacting a cell with the peptide decreases proliferation of the cell relative to a control cell not contacted with the peptide (or inhibits neovascularization relative to a control; claims 12 and 41).

Applicants note that the test of enablement is "whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with the information known in the art without undue experimentation." *Hybritech, Inc. v.*

Monoclonal Antibodies, Inc. 802 F.2d. 1318 (Fed. Cir. 1985). The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Applicants' specification meets this standard.

The specification describes that a peptide with the amino acid sequence EATVGERVRL (SEQ ID NO:2) inhibits VEGF induced proliferation of microvascular endothelial cells and pulmonary artery endothelial cells (see, e.g., paragraphs 89 and 90) and inhibits neovascularization in an ischemic retinopathy model (see, e.g., paragraph 91). The peptides encompassed by claim 12 and used in the method of claim 18 as amended are peptides of 5 to 20 amino acids and are required to be structurally related to the sequence of SEQ ID NO:2 (they must include a sequence that, over its full length, is at least 82% identical to the sequence of SEQ ID NO:2) and are required to share function with the peptide having the sequence of SEQ ID NO:2 (the peptide of the claim must decrease proliferation of a cell relative to a control cell not contacted with the peptide or inhibit neovascularization relative to a control). The specification also provides *in vitro* and *in vivo* assays to determine the function of a peptide (e.g., the cell culture and ischemic retinopathy assays described in paragraphs 89-91).

Moreover, generating peptides of 5 to 20 amino acids that include a sequence that is at least 82% identical, over its full length, to the sequence of SEQ ID NO:2 requires

nothing more than techniques standard in the art. In this regard, the specification, in paragraph 40, teaches:

The functional derivatives of the present invention can be synthesized chemically or produced through recombinant DNA technology. All these methods are well known in the art.

Clearly, in view of the teachings in Applicants' specification and the knowledge in the art, one skilled in the art could readily modify the peptide of SEQ ID NO:2 to arrive at the peptides encompassed by the claims and could test the function of such peptides using standard methods including those taught in the specification.

On this point Applicants further note that the specification, in Example 1, teaches how to make and use other peptide antagonists of VEGFR (to different regions of VEGFR). In fact, Applicants' specification provides specific examples of antagonist peptides to other cytokine receptors including IGF-1R, IL-4R, and IL-1R (see Table 1 and Examples 2-4). Accordingly, Applicants submit that specification enables one skilled in the art to make and use not just the peptide of SEQ ID NO:2, but all the peptides encompassed by the present claims.

For the above reasons, Applicants submit that one skilled in the art could make and use the antagonists of claim 12 and the methods of claim 18 without undue experimentation. The rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement should be withdrawn.

Written Description

The Office states (page 6):

The instant specification does not describe all possible functional derivations from all possible flexible regions of all possible cytokine receptors, including the nature or location of such derivations. Thus, the claims are drawn to a genus of "derived" peptides that have not been adequately described in the specification ...[T]he claims are also drawn to a genus of human VEGFR antagonists derived from all possible VEGFR polypeptides ... Because the claims do not identify human VEGFR by [a] specific sequence identifier, the claims read on any and all possible VEGFR sequences, and this genus of sequences has also not been adequately described in the instant specification.

Applicants address this basis for rejection, as it applies to the amended claims, as follows.

The Written Description Guidelines as published in the Federal Register (Vol. 66, No. 4, January 5, 2001, pages 1099-1111), with regard to a claim directed to a genus, state:

For each claim drawn to a genus: The written description requirement for a claimed genus may be satisfied ... by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Applicants submit that the claims as amended meet this standard.

As noted above, the peptides recited in claims 12 and 18, as amended, are peptides of 5 to 20 amino acids and are required to include a sequence that, over its full length, is at least 82% identical to the sequence of SEQ ID NO:2 and, therefore, the peptides encompassed by claims 12 and 18 are structurally related to the sequence of SEQ ID

NO:2. Further, in accordance with the claims, the peptides must function to decrease proliferation of a cell relative to a control cell not contacted with the peptide (or inhibit neovascularization). Consequently, the peptides must also be functionally related.

The specification, for example, in paragraphs 89 and 90, describes that a peptide having the sequence of SEQ ID NO:2 inhibits VEGF induced cell proliferation, and, for example, in paragraph 91, describes that a peptide having the sequence of SEQ ID NO:2 inhibits neovascularization. Moreover, the specification, for example, in paragraph 38 describes functional derivatives of peptides. For instance, as stated in paragraph 38, "derivatives include amino acid sequences having substitutions, deletions, or additions of one or more amino acids, provided that the biological activity of the protein is conserved." The specification also teaches that "functional derivatives of the present invention can be synthesized chemically or produced through recombinant DNA technology" (paragraph 40).

Applicants submit that, in view of the specification describing a particular antagonist having the sequence of SEQ ID NO:2 and describing that functional derivatives of such peptides are included in the invention, as well as how to make such functional derivatives, one skilled in the art would recognize that Applicants were in possession of the peptides encompassed by claims 12 and 18, as amended, at the time of filing. The written description rejection of claims 12 and 18, and their dependent claims, should be withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 13, 18, 23, and 27 are rejected under 35 U.S.C. § 112, second paragraph for reciting the acronym "VEGFR" and for not clearly identifying the VEGFR sequences encompassed by the claims. As noted above, claims 13, 23, and 27 have been canceled and rejection of these claims is moot. Claim 12, as amended, recites that VEGFR stands for vascular endothelial growth factor receptor. As such, Applicants submit that the meaning of VEGFR in the later claims is clear. This basis for rejection should be withdrawn.

Claims 18, 23, and 27 are rejected under 35 U.S.C. § 112, second paragraph because the metes and bounds of the terms "targeting" and "activity" are unclear and for omitting essential steps. Claims 23 and 27 have been canceled and rejection of these claims therefore is moot. The claims, as amended, no longer recite the term "targeting" and claim 18 now includes the step of contacting a cell with a peptide and recites that a decrease in proliferation of the cell relative to a control cell is indicative of the peptide inhibiting VEGFR activity. Applicants submit that the claims as amended are free of the 35 U.S.C. § 112, second paragraph, rejection.

Rejection under 35 U.S.C. § 102

Claims 12 and 13 are rejected under 35 U.S.C. § 102(b) as being anticipated by

Tan et al. (FEBS Letters 494:150-156, 2001; "Tan") or Binétruy-Tournaire et al. (EMBO

J. 19:1525-1533, 2000; "Binétruy-Tournaire"). Claims 12, 13, 18, 23, and 27 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,712,380 ("the '380 patent") or by U.S. Patent No. 5,952,199 ("the '199 patent"). Claims 13, 23, and 27 have been canceled and, therefore, rejection of these claims is moot. Applicants, for the reasons set forth below, submit that the claims as amended are free of these bases for rejection.

As noted above, claims 12 and 18 recite a peptide of 5 to 20 amino acids and to include a sequence that, over its full length, is at least 82% identical to the amino acid sequence EATVGERVRL (SEQ ID NO:2). None of the cited references describes a peptide having all of the features required by claim 12 as amended or its dependent claims. In particular, the sequences in the '380 patent and the '199 patent cited by the Office are not peptides 5 to 20 amino acids, but rather much longer sequences (668 and 767 amino acids, respectively). Similarly, neither Tan nor Binétruy-Tournaire describes a peptide of 5 to 20 amino acids including a sequence that, over its full length, is at least 82% identical to the sequence of SEQ ID NO:2.

In sum, none of the cited references describes each and every element required by the claims as amended. Applicants therefore submit that the present claims are free of the 35 U.S.C. § 102 rejection over the cited art. This basis for rejection should be withdrawn.

CONCLUSION

Applicants submit that the application is now in condition for allowance, and this action is hereby respectfully requested.

Enclosed is a Petition to extend the period for replying to the Office Action for three (3) months, to and including October 30, 2007, and a check in payment of the required extension fee.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Date: //ph//c/30, 200

Clark & Elbing LLP 101 Federal Street Boston, MA 02110

Telephone: 617-428-0200 Facsimile: 617-428-7045

Respectfully submitted,

Kristina Bieker Brady Ph.D

Reg. No. 39,109